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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,263	CANTOR, THOMAS L.	
	Examiner	Art Unit	
	GARY W. COUNTS	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31, 34 and 36-65* is/are pending in the application.

4a) Of the above claim(s) *1-26,34,37 and 41-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-31,36 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/27/07 has been entered.

Currently, claims 1-31, 34 and 36-65 are pending. Claims 1-26, 34, 37 and 41-65 are withdrawn as being directed to non-elected inventions. Claims 27-31, 36 and 38-40 are under examination.

Withdrawn Rejections

All rejections of claims not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 27-31, 36, and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim recites a method of guiding therapeutic decisions for a subject afflicted with an auto antibody for a natural substance. However, the body of the claim does not recite positive steps for guiding nor does the body of the claim provide any correlation to guiding or how guiding is provided. It is unclear how basing therapeutic decisions on the presence of the auto antibody provides guidance for a therapeutic decision.

Claim 27 is vague and indefinite because it is unclear how the presence of the auto antibody guides therapeutic decisions for the subject. The claim recites "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance to said subject on the presence of said auto antibody". However, "basing therapeutic decisions" is an interpretive clause that does not positively recite how a decision is made and how the results of the test are correlated to the guidance of the therapeutic decision. Does the mere presence of the auto antibody in the sample initiate, terminating and adjusting the level all at the same time? How does this mere presence correlate with initiating, terminating and adjusting as instantly recited? Is the presence compared to a standard or control and an increase or decrease as compared to the control provide guidance? The claims are read in light of the specification and limitations from the specification are not read into the claims.

Claim 27 step c) the recitation "the level of therapeutic administration" there is insufficient antecedent basis for this limitation.

Claim 28 the recitation “the medical condition” there is insufficient antecedent basis for this limitation.

Claim 28 the recitation “the underlying symptomology” there is insufficient antecedent basis for this limitation.

Claim 29 is vague and indefinite in reciting “wherein the natural substance is selected from the group provided in Table 2" because all of the substances disclosed in Table 2 appear to be drugs which have been manufactured by different companies and thus it is unclear how drugs which are produced from different substances and are not found naturally are considered to be a “natural substance”.

Claim 30 is vague and indefinite because it appears to contradict claim 27 from which is depends. Claim 27, step b) requires assessing the presence of the auto antibody. However, claim 30 recites the absence of the auto antibody is assessed, which contradicts the recitation in claim 27. Further, it is unclear how the absence of the auto antibody is correlated to guiding therapeutic decisions.

Claim 39 the recitation “low molecular weight label” is vague and indefinite. There is no definition provided for the phrase in the definition and it is unclear what is considered to be a low molecular weight label. Further, the recitation "low" is a relative term which renders the claim indefinite.

Claim 40 is vague and indefinite because of the recitation "capable of binding". Claim 39 from which claim 40 depends recites "bound by a low molecular weight label". The recitation of "capable of binding" claim 40 causes confusion because it is unclear if

applicant intends that a step is provided to enable binding to the natural substance after it is already bound or if Applicant intends something else.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 27, 28, 30 and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Lollar (US 2005/0079584).

Lollar discloses a method for determining if a patient comprises inhibitory antibodies (autoantibodies) (e.g. para. 0007, para. 0114) to hybrid factor VIII (natural substance). Lollar discloses treating the patient with factor VIII (para. 0114). Lollar discloses obtaining sample from the patient and assessing the sample for the presence of the antibodies (para. 0114). Lollar discloses that antibodies can be detected with an ELISA or radioimmunoassay (para. 0134). Lollar discloses that the factor VIII can be used in the method when the factor VIII contains at least one antigenic site (unhindered) and wherein the amount is sufficient for form a detectable complex with the inhibitory antibodies in the sample (para. 0134). Lollar also discloses that the amount of the

antibody in the test sample can be used to assist in the selection of medical therapies (para. 0038).

With respect to the recitation "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance to said subject on the presence of said auto antibody". The body of the claim recites an interpretive "basing therapeutic decisions" clause that is a non-manipulative mental step and does not inform the mechanics of how to guide or make decisions based on the presence of the autoantibodies. The clause does not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. The process steps that are positively recited in the claims provide for obtaining a sample from the patient and testing the sample for the presence of auto antibodies specific for the natural substance. Thus, Lollar reads on the claim because Lollar teaches obtaining a sample from the subject and testing the sample for the presence of auto antibodies specific for the natural substance and as stated above it is unclear how (see 112 2nd rejection above) the presence of the auto antibody guides therapeutic decisions for the subject or how a decision is made and how the results of the test are correlated to the guidance of the therapeutic decision.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 27, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conti-Fine (US 6,759,385) in view of Lollar (US 2005/0079584).

Conti-Fine discloses methods of detecting antibodies specific for endogenous antigen. Conti-Fine discloses the administration of endogenous protein (natural substance) or derivatives of the protein (analogs) to a subject (col 6, line 61 – col 7, line 30). Conti-Fine discloses assessing antibodies produced as a result of the administration of the protein or its derivative (analog)(col 2, lines 19-30, col 24, lines 12-26, col 90, lines 15-20, col 91, lines 30-37). Conti-Fine discloses making decisions on therapeutic administration (col 7, lines 43-52).

Conti-Fine differs from the instant invention in failing to specifically teach the auto antibody is not assessed via plasmon resonance.

Lollar discloses a method for determining if a patient comprises inhibitory antibodies (autoantibodies) (e.g. para. 0007, para. 0114) to hybrid factor VIII (natural substance). Lollar discloses treating the patient with factor VIII (para. 0114). Lollar discloses obtaining sample from the patient and assessing the sample for the presence

of the antibodies (para. 0114). Lollar discloses that antibodies can be detected with an ELISA or radioimmunoassay (para. 0134). Lollar discloses that the factor VIII can be used in the method when the factor VIII contains at least one antigenic site (unhindered) and wherein the amount is sufficient for form a detectable complex with the inhibitory antibodies in the sample (para. 0134).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate ELISA or radioimmunoassays into the method of Conti-Fine because Conti-Fine specifically teaches that the endogenous protein administered can be factor VIII and Conti-fine is generic with respect to how the antibodies are detected and Lollar teaches that it is known in the art to utilize assays such as ELISA or radioimmunoassays to detect antibodies which are developed due to the administration of an endogenous protein.

With respect to the recitation "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance to said subject on the presence of said auto antibody". The body of the claim recites an interpretive "basing therapeutic decisions" clause that is a non-manipulative mental step and does not inform the mechanics of how to guide or make decisions based on the presence of the autoantibodies. The clause does not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. The process steps that are positively recited in the claims provide for obtaining a sample from the patient and testing the sample for the presence of auto antibodies specific for the natural substance. Thus, the combination of Conti-fine and Lollar reads on the claim

because the combination of Conti-fine and Lollar teaches obtaining a sample from the subject and testing the sample for the presence of auto antibodies specific for the natural substance and as stated above it is unclear how (see 112 2nd rejection above) the presence of the auto antibody guides therapeutic decisions for the subject or how a decision is made and how the results of the test are correlated to the guidance of the therapeutic decision.

9. Claims 29 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conti-Fine in view of Lollar as applied to claims 27, 28 and 30 above, and further in view of Bunn (N. ENGL. J. Med. Vol 346, No. 7, pgs 522-523 2002).

See above for the teachings of Conti-Fine and Lollar.

Conti-Fine and Lollar differ from the instant invention in failing to teach the natural substance is erythropoietin.

Bunn describes a method of deciding to initiate or terminate administration of "erythropoietin" (p. 522, left column, third paragraph, first sentence, "[t]he article by Casadevall et al. in this issue of the Journal") based on an assessed autoantibody (p. 522, left column, third paragraph, second sentence, "immune response to epoietin") against both endogenous erythropoietin and recombinant erythropoietin (p. 522, right column, second paragraph, second sentence, "the antibody must react not only with epoietin but also with the small amount of endogenous erythropoietin").

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the modified method of Conti-Fine et al, to erythropoietin

because Conti-Fine is generic with respect to the endogenous protein for administration and according to Bunn, "about 3 million patients worldwide are being treated with epoetin" and because "[t]he clinical picture rapidly developing transfusion-dependent anemia is so dramatic that such cases are unlikely to escape attention (p. 522-523).

10. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lollar in view of Voller (Diagnostic Horizons, Dynasciences Corporation, Published by Microbiological Associates, Vol. 2, No. 1, pgs 1-7, 1978).

See above for the teachings of Lollar.

Lollar differs from the instant invention in failing to teach the autoantibody is assessed by a sandwich assay format.

Voller teaches that it is known in the art of ELISA assays to provide sandwich assay formats to determine a substance such as antibodies in a sample (e.g. p. 2, p. 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a sandwich assay format into the method of Lollar because Lollar specifically teaches that ELISA assay can be used to detect the antibodies and Lollar also teaches that reagents and methods are known to those skilled in the art (para. 0134) and Voller shows that sandwich assay formats are known for the detection of antibodies in a sample.

11. Claims 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lollar in view of Stevens (Clinical Immunology and Serology, A Laboratory Perspective, Chapter 10, Labeled Immunoassays, pages 144-146, 1996.)

See above for the teachings of Lollar.

Lollar differs from the instant invention in failing to teach labeling the natural substance and separating labeled autoantibody complex from the reaction mixture.

Stevens teaches that it is known in the art of immunoassays to label either the ligand or receptor and to provide separation steps to separate reacted complex from unreacted complexes prior to detection of the labeled complexes (pgs 145-146). Stevens teaches that the labels can be radioactive, enzymes and chemiluminescent labels (p. 146) (note same labels as disclosed by Applicant, therefore are low molecular weight labels).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate labels and separation steps such as taught by Stevens into the method of Lollar because Lollar specifically teaches that reagents and methods are known to those skilled in the art to detect antibodies in a sample(para. 0134) and Stevens teaches that it is well known in the art of immunoassays to label either the ligand or receptor and to provide separation steps to separate reacted complex from unreacted complexes prior to detection of the labeled complexes.

With respect to claim 40 as instantly recited. Since the combination of Lollar and Stevens teaches reagents consonant to those instantly claim. It is deemed the molecular weight of the low molecular weight label that is capable of binding the unhindered natural

substance comprises less than about 50%. Further, the optimum proportion of the molecular weight of the low molecular weight label versus the molecular weight of the unhindered natural substance itself can be determined by routine experimentation and thus is considered to be obvious to one of ordinary skill in the art. Also, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

Response to Arguments

12. Applicant's arguments filed 07/27/07 have been fully considered but they are not persuasive.

112 2nd rejections

Applicant argues that the preamble reciting a method of "guiding" decisions is not a limitation of the claimed invention and that skilled persons understand the phrase "basing therapeutic decisions as used in claim 27, step c). These arguments are not found persuasive because as stated above the body of the claim does not recite positive steps for guiding nor does the body of the claim provide any correlation to

guiding or how guiding is provided. The claim as recited does not make clear how basing therapeutic decisions correlates to guiding therapeutic decisions. Method claims should conclude with a step relating the method result to the purpose of the method in this case guidance for therapeutic decisions.

Art rejections

Applicant argues that Conti-Fine provides a therapeutic method to treat antibody-mediated diseases by administering an “epitope” peptide comprising an epitpoe sequence derived from a particular antigen associated with the antibody-mediated disease (col 2, lines 9-13). Applicant states that the method is effective to specifically tolerize, or down-regulate, the immune response to the antigen and significantly, the "epitope" peptide does not include the entire sequence of the antigen (Conti -Fine col 2, lines 13-18). Applicant states thus, the "epitope” peptide is not a "natural substance" within the scope of claim 27. This is not found persuasive because claim 27 also recites analogs of the natural substance and the current specification does not provide a definition for analog and given its broadest reasonable interpretation the peptide of Conti-Fine which includes portions of the sequence of the antigen would be considered to be an analog of the natural substance. Further, Conti-Fine specifically teaches that the substance which is administered can be the endogenous protein itself (natural substance) col 6, line 61 – col 7, line 48).

Applicant argues that Conti-Fine does not assess an autoantibody. This is not found persuasive because Conti-Fine assays antibodies against specific peptides (e.g.

col 24, lines 21-23, “the amount of antibody specific for the antigen obtained at time periods before immunization and after immunization”) because Conti-Fine wishes to define the antibody specificity and to determine whether these same antibodies are specific for “natural substance” (e.g. col. 2, lines 19-30, col 90, lines 16-20, col 91, lines 30-37(anti-VIII antibody concentrations to “self”). Conti-Fine describes several types of “natural substances", including therapeutically administered natural substances in general, and acetylcholine receptors in particular. Thus, Conti-Fine assay auto antibodies specific for “natural substances” or the peptides "analogs".

Applicant argues that the portions of Conti-Fine cited by the Examiner simply do not teach a method of basing therapeutic decisions to initiate, terminate or adjust the level of therapeutic administration of a natural substance based on the presence of an assessed auto antibody to said natural substance, as claimed. This is not found persuasive because as stated above the body of the claim recites an interpretive “basing therapeutic decisions” clause that is a non-manipulative mental step and does not inform the mechanics of how to guide or make decisions based on the presence of the autoantibodies. The clause does not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. The process steps that are positively recited in the claims provide for obtaining a sample from the patient and testing the sample for the presence of auto antibodies specific for the natural substance. Thus, the combination of Conti-fine and Lollar reads on the claim because the combination of Conti-fine and Lollar teaches obtaining a sample from the subject and testing the sample for the presence of auto antibodies specific for the

natural substance and as stated above it is unclear how (see 112 2nd rejection above) the presence of the auto antibody guides therapeutic decisions for the subject or how a decision is made and how the results of the test are correlated to the guidance of the therapeutic decision.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

8/15/09